Please amend claim 6 as follows:

--6. (Amended) A method according to claim 1, wherein the detection method comprises PCR amplification of the *GH1* gene of the individual using (a) a *GH1* gene-specific fragment, being a fragment unique to the *GH1* gene whose sequence is not found in the four other paralogous (non-*GH1*) genes in the GH cluster, and (b) one or more *GH1* gene-specific primers which cannot bind to the homologous flanking regions in the four other paralogous (non-*GH1*) genes in the GH cluster.

a3

Please amend claim 7 as follows:

--7. (Amended) A method according to claim 1, wherein the detection method comprises PCR amplification of the entire *GH1* gene of the individual and nested PCR of overlapping constituent fragments of the *GH1* gene of the individual. --

a4

Please amend claim 8 as follows:

--8. (Amended) A method according to claim 1, wherein the detection method comprises PCR amplification of all or a fragment of genomic DNA spanning the Locus Control Region of the *GH1* gene.--

a5

Please amend claim 9 as follows:

--9. (Amended) A method according to claim 1, wherein the detection method comprises mutational screening of all or a fragment of the individual's *GH1* gene by DHPLC.--

a6

Please amend claim 11 as follows:

--11. (Amended) A detection method according to claim 10, which detection method further comprises the use of one or more primer(s) selected from:

CTC CGC GTT CAG GTT GGC (GH1DF);

AGG TGA GCT GTC CAC AGG (GH1DR);

GGG CAA CAG TGG GAG AGA AG (GH2DF);

CCT CCA GGG ACC AGG AGC (GH2DR);

CAT GTA AGC CCA GTA TTT GGC C (GH3DF);

CTG AGC TCC TTA GTC TCC TCC TCT (GH3DR);

GAC TTT CCC CCG CTG GGA AA (GH4DF);

GGA GAA GGC ATC CAC TCA CGG (GH4DR);

TCA GAG TCT ATT CCG ACA CCC (GH5DF);

GTG TTT CTC TAA CAC AGC TCT C (GH5DR);

TCC CCA ATC CTG GAG CCC CAC TGA (GH6DF)

CGT AGT TCT TGA GTA GTG CGT CAT CG (GH6DR);

TTC AAG CAG ACC TAC AGC AAG TTC G (GHD7F);

CTT GGT TCC CGA ATA GAC CCC G (GH7DR);

GTGCCCCAAGCCTTTCCC (LCR15: 1159-1177);

TGTCAGATGTTCAGTTCATGG (LCR13: 1391-1412);

CCTCAAGCTGACCTCAGG (LCR25: 1346-1363);

GATCTTGGCCTAGGCCTCG (LCR23: 1584-1602);

LCR 5A (5' CCAAGTACCTCAGATGCAAGG 3');

LCR 3.0 (5' CCTTAGATCTTGGCCTAGGCC 3');

LCR 5.0 (5' CCTGTCACCTGAGGATGGG 3');

LCR 3.1 (5' TGTGTTGCCTGGACCCTG 3');

LCR 3.2 (5' CAGGAGGCCTCACAAGCC 3')

Cont A7

LCR 3.3 (5′ ATGCATCAGGGCAATCGC 3′);

GH1G5 (5′ GGTACCATGGCTACAGGTAAGCGCC 3′);

GH1G3 (5′ CTCGAGCTAGAAGCCACAGCTGCCC 3′);

BGH3 (5′ TAGAAGGCACAGTCGAGG 3′);

GH1R5 (5′ ATGGCTACAGGCTCCCGG 3′); and

GH1R3 (5′ CTAGAAGCCACAGCTGCCC 3′).--

Please amend claim 12 as follows:

--12. (Amended) A variant of *GH1*, which differs from *GH1* and is detected by or is detectable by a method according to claim 1 but was not detected by methods used hitherto, such as those reliant on patient selection criteria based primarily on absolute height.--

A8

Please amend claim 14 as follows:

--14. (Amended) A variant of *GH1* according to claim 12 comprising a missense mutation.--

A9

Please amend claim 15 as follows:

--15. (Amended) A variant of *GH1* according to claim 12 comprising a silent mutation which affects the activity of the signal peptide.--

A10

Please amend claim 17 as follows:

--17. (Amended) A protein or amino acid sequence encoded by a variant of *GH1* according to claim 12.--

A11

Please amend claim 21 as follows:

--21. (Amended) A screening method for screening an individual suspected of GH dysfunction, which screening method comprises the steps of:

(a) obtaining a test sample comprising a nucleotide sequence of the human *GH1* gene from the individual; and

(b) comparing a region of the sequence obtained from the test sample with the corresponding region of a predetermined sequence

wherein the predetermined sequence is selected from a variant of *GH1* according to claim 12.--

Amend claim 24 as follows:

--24. (amended) A screening method according to claim 21, comprising:

(a) obtaining a first test sample from an individual; and

(b) comparing the *GH1* gene or *GH1* transcript, or fragment therefrom (*eg* cDNA), in the first test sample to the corresponding gene, transcript or fragment of a *GH1* variant obtainable from a second test sample derived from an individual exhibiting the following criterion:

(i) growth failure defined as a growth pattern [delineated by a series of height measurements; Brook CDG (Ed) Clinical Paediatric Endocrinology 3rd Ed, Chapter 9, p141 (1995, Blackwell Science)] which, when plotted on a standard height chart [Tanner *et al* Arch. Dis. Child 45 755-762 (1970)], predicts an adult height for the individual which is outside the individual's estimated target adult height range, the

Cont a'3

estimate being based upon the heights of the individual's parents.--

Amend claim 26 as follows:

--26. (amended) A screening method according to claim 21 in which simultaneous screens are used either for multiple known mutations or for all possible mutations by hybridization of a labelled sample of DNA (cDNA or genomic DNA derived from the individual) to micro-arrays of mutation-specific oligonucleotide probes immobilised on a solid support.--

A14

Amend claim 28 as follows:

--28. (amended) A kit suitable for use in carrying out a screening method according to claim 21, which kit comprises:

A15

(a) an oligonucleotide having a nucleic acid sequence corresponding to a region of a *GH1* variant, which region incorporates at least one variation from the corresponding wild-type hGH gene sequence; and/or

(b) an oligonucleotide having a nucleic acid sequence corresponding to the wild-type hGH gene sequence in the region specified in (a); and, optionally,

(c) one or more reagents suitable for carrying out PCR for amplifying desired regions of the individual's DNA.--

Cancel claim 29.--

--30. (amended) A kit according to claim 28, wherein kit component (a) comprises a plurality of said oligonucleotides immobilised on a solid support.--

--31. (amended) A kit suitable for use in carrying out a detection method in which the variant is at least one of the variants claimed in claim 12.--

Amend claim 32 as follows:

--32. (amended) A screening method for screening an individual suspected of GH dysfunction, which screening method comprises the steps of:

(a) obtaining a test sample comprising an amino acid sequence encoded by the human *GH1* gene of the individual; and

(b) analysing the test sample for the presence of a GH variant wherein the GH variant is selected from those according to claim 17.--

Amend claim 34 as follows:

--34. (amended) An isolated, purified or recombinant nucleic acid sequence selected from:

(a) a sequence comprising a variant of *GH1* according to claim 12 or

(b) a sequence substantially homologous to or that hybridises to sequence (a) under stringent conditions; or

(c) a sequence substantially homologous to or that hybridizes under stringent conditions to the sequence (a) or (b) but for the degeneracy of the genetic code; or

(d) an oligonucleotide specific for any of the sequences (a), (b) or (c).--

--37. (amended) A process for preparing a variant of *GH1* according to claim 12, which process comprises:

(i) culturing a host cell; and

(ii) recovering from the culture medium the variant of *GH1* thereby produced.--

Amend claim 38 as follows:

--38. (amended) An amino acid sequence encoded or expressed by a sequence, vector, or cell as defined in claim 34 in culture medium.--

Amend claim 39 as follows:

--39. (amended) A composition comprising a variant of *GH1* or a GH variant according to claim 12, respectively, in association with a pharmaceutically acceptable carrier therefor.--

Amend claim 40 as follows:

--40. (amended) Use of a variant of *GH1* or a GH variant according to claim 12, respectively, for a therapeutic, diagnostic or detection method.--

Cancel claim 42.

Cancel claim 43.

Amend claim 44 as follows: